

Amendments to the Specification:

Please replace the paragraph beginning on page 1, line 4, with the following amended paragraph:

This application **is a continuation of U.S. Patent Application Serial No. 10/172,388, filed June 14, 2002, which** is a continuation of U.S. Patent Application Serial No. 09/550,302, filed April 14, 2000, which is a continuation-in-part of U.S. application serial no. 09/130,886, filed August 7, 1998, now U.S. Patent No. 6,255,289, which is a continuation of U.S. application serial no. 08/591,197, filed January 16, 1996, now U.S. Patent No. 5,885,971, which is a continuation-in-part of U.S. application serial no. 08/410,660, filed March 24, 1995, now U.S. Patent No. 5,837,693, which applications are incorporated herein by reference.

Please replace the paragraph beginning on page 3, line 6, with the following amended paragraph:

The invention features methods for delivering a polypeptide to the bloodstream of a subject by introduction of a nucleic acid construct into secretory gland ~~eells~~(~~e.g.~~, **cells (e.g.,** cells of salivary gland, pancreas, or liver). In general, the method involves introduction of a nucleic acid construct into a secretory gland duct, which introduction results in expression of a gene product encoded by the introduced construct and delivery of the gene product into the bloodstream of the subject.

Please replace the paragraph beginning on page 22, line 4, with the following amended paragraph:

Alternatively or in addition, the DNA of interest can be complexed with polycationic substances such as poly-L-lysine or ~~DEAC-dextran~~ **DEAE-dextran**, targeting ligands, and/or DNA binding proteins (e.g., histones). DNA- or RNA-liposome complex formulations comprise a mixture of lipids which bind to genetic material (DNA or RNA) and facilitate delivery of the nucleic acid into the cell. Liposomes which can be used in accordance

with the invention include DOPE (dioleoyl phosphatidyl ethanol amine), CUDMEDA (N-(5-cholestrum-3- β -ol 3-urethanyl)-N',N'-dimethylethylene diamine).

Please replace the paragraph beginning on page 22, line 11, with the following amended paragraph:

Lipids which can be used in accordance with the invention include, but are not limited to, DOPE (Dioleoyl phosphatidylethanolamine), ~~cholesterol~~, and cholesterol, and CUDMEDA (N-(5-cholestrum-3-ol 3 urethanyl)-N',N'-dimethylethylenediamine). As an example, DNA can be administered in a solution containing one of the following cationic liposome formulations: LipofectinTM (LTI/BRL), TransfastTM (Promega Corp), Tfx50TM (Promega Corp), Tfx10TM (Promega Corp), or Tfx20TM (Promega Corp). The concentration of the liposome solutions range from about 2.5% to 15% volume:volume, preferably about 6% to 12% volume:volume. Further exemplary methods and compositions for formulation of nucleic acid (e.g., DNA, including DNA or RNA not contained within a viral particle) for delivery according to the method of the invention are described in U.S. Pat. Nos. 5,892,071; 5,744,625; 5,925,623; 5,527,928; 5,824,812; 5,869,715.

Please replace the paragraph beginning on page 37, line 4, with the following amended paragraph:

Approximately 48 hours after cDNA or saline injection, the animals were again anesthetized and a tracheostomy performed. A control blood sample was drawn from the femoral vein of each animal. McH was administered at 0.8 mg/kg body weight by subcutaneous injection. Twenty minutes after McH injection, saliva and blood samples were collected from each animal. The blood samples were collected from the inferior vena cava and by heart puncture. Serum was separated from the blood of all samples after clotting, and kept at 20°C prior to assay. In addition, the salivary glands and a portion of the pancreas were removed and homogenized in 50 mM phosphate buffer (pH 8.0) 1:10 w/v. The homogenates were spun at

50,000 x g for 1 h and the supernatant stored at 20°C. A small portion of parotid salivary glands were fixed in 10% buffered formalin and saved for histologic examination. The parotid glands showed no observable signs of inflammation as a result of cDNA injection.